



Agency for Healthcare Research and Quality
Advancing Excellence in Health Care



NATIONAL
GUIDELINE
CLEARINGHOUSE

General

Guideline Title

A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing.

Bibliographic Source(s)

Boullata JI, Gilbert K, Sacks G, Labossiere RJ, Crill C, Goday P, Kumpf VJ, Mattox TW, Plogsted S, Holcombe B, American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. JPEN J Parenter Enteral Nutr. 2014 Mar;38(3):334-77. [196 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions for the grading of recommendations (Strong, Weak, Further research needed) are provided at the end of the "Major Recommendations" field.

Does Education of Prescribers Improve Parenteral Nutrition (PN) Ordering?

The guideline developers suggest providing education to healthcare professionals to improve PN ordering, thereby reducing errors.

GRADE: Weak

What Is the Maximum Safe Osmolarity of PN Admixtures Intended for Peripheral Vein Administration?

The guideline developers suggest that PN with an osmolarity of up to 900 mOsm/L can be safely infused peripherally. Higher osmolarity limits, especially when peripheral PN is prepared as a total nutrient admixture (TNA), may also be tolerated, but the evidence to support a safe limit is lacking.

GRADE: Weak

What Are the Appropriate Calcium Intake and Calcium-Phosphate Ratios (Ca:P) in PN for Optimal Neonatal Bone Mineralization?

The guideline developers recommend an elemental calcium intake of 76 mg/kg per day for short-term PN in neonates.

GRADE: Strong

The guideline developers suggest a Ca:P ratio of 1.7:1 (mg:mg) or 1.3:1 (mmol:mmol) in short-term PN in neonates.

GRADE: Weak

What Are the Clinical Advantages or Disadvantages of Commercially Available Premade ("Premixed") Multichambered PN Formulations Compared With Compounded PN Formulations?

The guideline developers suggest that commercially available premade multichambered PN products be considered as an available option for patients alongside compounded (customized or standardized) PN formulations to best meet an organization's patient needs.

GRADE: Weak

What Are the Clinical (Infection, Catheter Occlusion) Advantages or Disadvantages of 2-in-1 Compared With 3-in-1 PN Admixtures?

The guideline developers suggest that there is no clinical difference in infectious complications between the two PN delivery systems; 3-in-1 formulations administered in the homecare setting may increase the risk for catheter occlusion and shorten catheter lifespan.

GRADE: Weak

What Macronutrient Dosing Limits Are Expected to Provide for the Most Stable 3-in-1 Admixtures?

The guideline developers recommend that total nutrient admixtures maintain final concentrations of amino acid $\geq 4\%$, monohydrated dextrose $\geq 10\%$, and injectable lipid emulsion $\geq 2\%$ to be more likely to remain stable for up to 30 hours at room temperature (25°C) or for 9 days refrigerated (5°C) followed by 24 hours at room temperature.

GRADE: Strong

What Are the Most Appropriate Recommendations for Optimizing Calcium (Gluconate) and (Na- or K-) Phosphate Compatibility in PN Admixtures?

The guideline developers cannot make a recommendation due to the multiple variations in amino acid concentrations, PN volume, pH, presence or absence of fat emulsion, and the amounts of other minerals (e.g., magnesium). The guideline developers suggest that published graphs for specific products provide adequate guidance; however, no evidence indicates that these formulations remain stable for >24 to 48 hours.

GRADE: Weak

What Micronutrient Contamination Is Present in Parenteral Stock Solutions Currently Used to Compound PN Admixtures?

The guideline developers suggest that, given the level of mineral contamination found in parenteral stock solutions used to compound PN admixtures, practitioners purchase products that accurately describe levels of contamination and also take that exposure into account when recommending or reviewing trace element dosing.

GRADE: Weak

Is it Safe to Use the PN Admixture as a Vehicle for Non-Nutrient Medication Delivery?

The guideline developers recommend that non-nutrient medication be included in PN admixtures *only* when supported by (1) pharmaceutical data describing physicochemical compatibility and stability of (a) the additive medication and (b) the final preparation under conditions of typical use, and (2) clinical data confirming the expected therapeutic actions of the medication. Extrapolation beyond the parameter limits (e.g., products, concentrations) of the given data is discouraged.

GRADE: Strong

Should Heparin Be Included in the PN Admixture to Reduce the Risk of Central Vein Thrombosis?

The guideline developers suggest that heparin not be included in PN admixtures for reducing the risk of central vein thrombosis in adults.

GRADE: Weak

What Methods of Repackaging Intravenous Fat Emulsion (IVFE) Into Smaller Patient-Specific Volumes Are Safe?

The guideline developers recommend against the repackaging of IVFE into syringes for administration to patients. The guideline developers suggest that other methodologies for repackaged IVFE, such as drawn-down IVFE units, are preferable.

GRADE: Strong

What Beyond-Use Date (BUD) Should be Used for (a) IVFE Dispensed for Separate Infusion in the Original Container and (b) Repackaged IVFE?

- a. The guideline developers recommend that the BUD for unspiked IVFE in the original container should be based on the manufacturer's provided information. The BUD for IVFE in the original container spiked for infusion should be 12 to 24 hours.
- b. Although repackaged IVFE is not recommended, when used, the BUD for IVFE transferred from the original container to another container for infusion separately from a 2-in-1 PN solution should be 12 hours.

GRADE: Strong

Definitions:

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. A full description of the methodology has been published in the A.S.P.E.N. guideline "Clinical Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients: Applying the GRADE System to Development of A.S.P.E.N. Clinical Guidelines" (see the "Availability of Companion Documents" field).

Strength of Recommendation

Strong	Net benefits outweigh harms
Weak	Tradeoffs for patient are important
Further Research Needed	Uncertain tradeoffs

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Any condition requiring parenteral nutrition (PN)

Guideline Category

Management

Clinical Specialty

Critical Care

Internal Medicine

Nursing

Nutrition

Pharmacology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Hospitals

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

To provide evidence-based guidance for clinical practices involving parenteral nutrition (PN) prescribing, order review, preparation, and administration

Target Population

Neonates, children, and adults receiving parenteral nutrition (PN) in a variety of settings

Interventions and Practices Considered

1. Education for healthcare professionals to improve parenteral nutrition (PN) ordering
2. Application of safe osmolality criteria for PN admixtures
3. Application of appropriate PN calcium intake and calcium-phosphate ratios (neonates)
4. Consideration of commercially available premade multichambered PN products
5. Application of macronutrient dosing limits criteria for 3-in-1 PN admixtures
6. Use of published graphs for specific product guidance
7. Purchase of products that accurately describe levels of contamination
8. Inclusion of non-nutrient medications in PN admixtures only when supported by pharmaceutical and clinical data
9. Avoidance of heparin in in PN admixtures for central vein thrombosis risk
10. Avoidance of repackaging intravenous fat emulsion (IVFE) into syringes for administration to patients
11. Determining beyond-use date (BUD) based on the manufacturer's provided information

Major Outcomes Considered

- Administration errors with inadvertent overdose
- Risk of microbial contamination
- Medication errors

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Description of Methods Used to Collect/Select the Evidence

For the current Clinical Guideline, searches of PubMed, EMBASE, International Pharmaceutical Abstracts (IPA), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) from 1970 to June 2013 were performed to identify pertinent studies. References from older papers were also searched. The search excluded foreign languages. Inclusion criteria were in vitro and in vivo studies, and adult, pediatric, and neonatal patients.

Search terms were neonates, parenteral nutrition, calcium, phosphorus, solubility adult, pediatric, peripheral parenteral nutrition, osmolality, phlebitis, total nutrient admixture, 3-in-1, 2-in-1, IV fat emulsion, IV lipids, lipid emulsions, stability, soybean oil, safflower oil, lipid particle size, zeta potential, temperature, amino acids, dextrose, storage, total parenteral nutrition, hyperalimentation, compatibility, medication, [individual drugs listed] heparin, thrombus, venous thrombosis, prescriber education, parenteral nutrition order, error reduction, calcium-phosphorus ratio, bone mineralization, commercially available multi-chamber PN formulations, macronutrient dosing, micronutrient contamination, phlebitis, catheter infection, repackaging fat emulsion, beyond-use-date, catheter occlusion, compounding, contamination, dietitians, dispensing, education, healthcare professionals, infection, labeling, micronutrient, nurse, osmolality, pharmacist, physician, prescribing.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Note: The American Society for Parental and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. A full description of the methodology has been published in the A.S.P.E.N. guideline "Clinical Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients: Applying the GRADE System to Development of A.S.P.E.N. Clinical Guidelines" (see the "Availability of Companion Documents" field).

The Quality of Evidence

Quality	Definition
High	Further research is very unlikely to change the guideline developers' confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on the guideline developers' confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on the guideline developers' confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

A systematic review of the best available evidence was used by an expert work group to answer a series of questions about parenteral nutrition

(PN) prescribing, order review, compounding, labeling, and dispensing. Concepts from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) format were applied as appropriate.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. Briefly, specific clinical questions where nutrition support is a relevant mode of therapy are developed and key clinical outcomes are identified. A rigorous search of the published literature is conducted, each included study is assessed for research quality, tables of findings are developed, and the body of evidence for the question is evaluated and graded. Randomized controlled clinical trials are initially graded as strong evidence but may be downgraded in quality based on study limitations. Controlled observational studies are initially graded as weak evidence but may be graded down further based on study limitations or upgraded based on study design strengths. In a consensus process, the authors make recommendations for clinical practice that are based on the evidence review assessed against consideration of the risks and benefits to patients. Recommendations are graded as strong when the evidence is strong and/or the risk vs benefit analysis is strong. Weak recommendations may be based on weaker evidence and/or weaker trade-offs to the patient. When limited research is available to answer a question, the recommendation is for further research to be conducted.

Evaluating the safety of nutrition preparations and products often requires data derived from in vitro studies. Some of the vital safety-related questions with patient outcome implications that made use of in vitro evidence were included in this document. For example, in vitro data are necessary to evaluate stability, compatibility, and sterility. Although these studies do not align with the GRADE process, they are just as critical to the integrity of safe parenteral nutrition (PN) use in clinical practice. In these cases, the work group still conducted literature searches evaluated the study quality, and provided evidence tables. Manuscripts were uniformly evaluated against quality criteria and are provided in the tables of evidence. The strength of recommendations based on in vitro data follows author considerations for potential risks to patients as well as the available evidence.

Rating Scheme for the Strength of the Recommendations

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. A full description of the methodology has been published in the A.S.P.E.N. guideline "Clinical Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients: Applying the GRADE System to Development of A.S.P.E.N. Clinical Guidelines" (see the "Availability of Companion Documents" field).

Strength of Recommendation

Strong	Net benefits outweigh harms
Weak	Tradeoffs for patient are important
Further Research Needed	Uncertain tradeoffs

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The Clinical Guideline authors, who represent a range of academic and clinical expertise, are involved in prescribing, reviewing, compounding, or labeling and dispensing parenteral nutrition (PN). The external and internal expert reviewers, including the American Society of Parenteral and Enteral Nutrition Board of Directors, have a similar, but even broader breadth of professional expertise.

The specific clinical guideline recommendations were developed using consensus prior to review and approval by the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of parenteral nutrition (PN) in neonates, children, and adults maximizes clinical benefit while minimizing the potential risk for adverse events

Potential Harms

- Many clinicians find that "premixed" parenteral nutrition (PN) formulations often will not meet the caloric, amino acid, and electrolyte needs of critically ill patients, who are often obese, require fluid restriction, and display hepatic/renal dysfunction. These products have particularly been criticized for their high dextrose concentrations, which could increase the risk of hyperglycemia and infection. Patient safety data are lacking for a reduction of errors associated with "premixed" PN products in relation to prescribing, compounding, and administration. "Premixed" PN formulations can be useful in appropriate patient populations when screened and assessed by suitably trained clinicians with expertise in nutrition support therapy.
- The primary drawback of the 3-in-1 PN system is that it requires a larger pore size filter (1.2 μm) and precludes the use of a 0.22- μm filter, which eliminates a greater amount of particulate matter including some bacteria. The 3-in-1 system also suffers from a higher risk for emulsion destabilization from inappropriate concentrations of nutrients as well as a greater incidence of medication incompatibility with the fat emulsion portion of the admixture.

Qualifying Statements

Qualifying Statements

These American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines are based upon general conclusions of health professionals who, in developing such Clinical Guidelines, have balanced potential benefits to be derived from a particular mode of medical therapy against certain risks inherent with such therapy. However, the professional judgment of the attending health professional is the primary component of quality medical care. Because guidelines cannot account for every variation in circumstances, the practitioner must always exercise professional judgment in the application of these guidelines. These Clinical Guidelines are intended to supplement, but not replace, professional training and judgment.

Implementation of the Guideline

Description of Implementation Strategy

The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) has developed a parenteral safety toolkit on their Web site (www.nutritioncare.org/pnsafety). It includes open access to these guidelines, as well as an accompanying parenteral nutrition safety consensus paper and a full toolkit of checklists, institutional safety tools, and ways to report errors.

Implementation Tools

Tool Kits

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Boullata JI, Gilbert K, Sacks G, Labossiere RJ, Crill C, Goday P, Kumpf VJ, Mattox TW, Plogsted S, Holcombe B, American Society for Parenteral and Enteral Nutrition. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. JPEN J Parenter Enteral Nutr. 2014 Mar;38(3):334-77. [196 references] [PubMed](#)

Adaptation

Not applicable. The guideline was not adapted from another source.

Date Released

2014 Mar

Guideline Developer(s)

American Society for Parenteral and Enteral Nutrition - Professional Association

Source(s) of Funding

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Guideline Committee

A.S.P.E.N. Clinical Guidelines Editorial Board

Composition of Group That Authored the Guideline

Authors: Joseph I. Boullata, PharmD, RPh, BCNSP, FASPEN; Karen Gilbert, RN, MSN, CNSC, CRNP; Gordon Sacks, PharmD, BCNSP, FCCP; Reginald J. Labossiere, MD; Cathy Crill, PharmD, BCNSP; Praveen Goday, MD, MBBS, CNSC; Vanessa J. Kumpf, PharmD, BCNSP; Todd W. Mattox, PharmD, BCNSP; Steve Plogsted, PharmD, BCNSP, CNSC; Beverly Holcombe, PharmD, BCNSP, FASHP; and the American Society for Parenteral and Enteral Nutrition

Financial Disclosures/Conflicts of Interest

Financial disclosure: None declared.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [Journal of Parenteral and Enteral Nutrition Web site](#) .

Availability of Companion Documents

The following is available:

- Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines. American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.); 2012 Jan. 5 p. Electronic copies: Available from the [Journal of Parenteral and Enteral Nutrition Web site](#) .

Additionally, a safety toolkit that includes checklists, institutional safety tools, and ways to report errors is available from the [American Society for Parenteral and Enteral Nutrition Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on June 25, 2014. The information was verified by the guideline developer on July 9, 2014.

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouse^{â„¢} (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion-criteria.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.